



ATTACHMENT A

Marked-Up Replacement Paragraphs

Please amend the marked paragraphs in the manner and locations set forth below:

Page 1, first paragraph, please amend the paragraph as follows:

Cross-Reference to Related Applications

The present application is a divisional application of U.S. Appln. Serial No. 09/386,962, filed August 31, 1999, now U.S. Patent No. 6,635,473, and claims the benefit of U.S. Provisional Applications Serial No. 60/117,119, filed January 25, 1999, and Serial No. 60/098,443, filed August 31, 1998.

Page 5, line 2, please amend the paragraph as follows:

It has also been discovered that in the A region of SdrF and SdrG there is highly conserved amino acid sequence that can be used to derive a consensus TYTFTDYVD (SEQ ID NO:16) motif. The motif can be used in multicomponent vaccines to impart broad spectrum immunity to bacterial infections, and also can be used to produce monoclonal or polyclonal antibodies that impart broad spectrum passive immunity. In an alternative embodiment, any combination of the variable sequence motif derived from the Sdr protein family, (T) (Y) (T) (F) (T) (D/N) (Y) (V) (D) (SEQ ID NO: 40), can be used to impart immunity or to induce protective antibodies. The proteins, or antigenic portions thereof, are used to produce antibodies for the diagnosis of coagulase-negative staphylococcal bacterial infections or for the development of anti-coagulase-negative staphylococcal vaccines for active or passive immunization. When administered to a wound or used to coat polymeric biomaterials *in vitro* and *in vivo*, both the protein and antibodies thereof are also useful as blocking agents to prevent or inhibit the binding of coagulase-negative staphylococci to the wound site or to any biomaterials. The SdrF, SdrG and SdrH proteins are further useful as scientific research tools to understand of the mechanisms of bacterial pathology and the development of antibacterial therapies.

Page 8, line 11, please amend the paragraph as follows:

Figure 5 shows the relationships between the Sdr proteins of *S. aureus* and *S. epidermidis* as follows: Fig. 5A is a schematic representation of previously described *S. aureus* Sdr proteins; Fig. 5B is a schematic representation of SdrF, SdrG, and SdrH showing the relative position and/or size of their signal sequences (S), region As (A), region B repeats (B_n), SD-repeat region (SD), region C (C) (SdrH only), and wall/membrane spanning regions (WM); and Fig. 5C represents the C-terminal amino acid sequences of SdrF (SEQ ID NO:18), SdrG (SEQ ID NO: 19), and SdrH (SEQ ID NO: 20) showing the positions of the SD repeats, LPXTG motif (underlined), hydrophobic membrane-spanning regions (bold), and charged terminal residues.

Page 10, line 20, please amend the paragraph as follows:

The disclosed extracellular matrix-binding proteins share a unique dipeptide repeat region (region R) including predominately aspartate and serine residues. This DS repeat is encoded by 18 nucleotide repeats with the consensus GAY TCN GAY TCN GAY AGY (SEQ ID NO: 15), with TCN as the first and second serine codons and AGY as the third serine codon. The R region is near the C-terminus of the proteins and typically contains between 40 and 300 DS residues; or more particularly, greater than 60, 80, 100, 120, 150, 200 or 250 repeating units, of which greater than 90, 95 or even 98% are the amino acids D or S. The R region DS repeat varies in length between proteins, and while the region R itself does not bind extracellular matrix proteins, the R region enables the presentation of the binding regions of the protein on the cell surface of *S. aureus*. Thus, probes to the consensus DNA encoding the DS repeat (see above) can be used to identify other genes encoding different binding proteins essential to the attachment of *S. aureus* to host tissues. Antibodies to an R region can also be used to identify such additional binding proteins.

Page 11, line 1, please amend the paragraph as follows:

It has been discovered that in the A region of SdrF and SdrG there is highly conserved amino acid sequence that can be used to derive a consensus TYTFTDYVD (SEQ ID NO:16) motif. The motif can be used in multicomponent vaccines to impart broad spectrum immunity to bacterial infections, and also can be used to produce monoclonal or polyclonal antibodies that impart broad spectrum passive immunity. In an alternative embodiment, any combination of the variable sequence motif derived from the Sdr protein family, (T) (Y) (T) (F) (T) (D/N) (Y) (V) (D) (SEQ ID NO: 40), can be used to impart immunity or to induce protective antibodies.

Page 40, line 18, please amend the paragraph as follows

Example 1

Identification of Sdr encoding genes in coagulase negative staphylococci

Five genes (*clfA*, *clfB*, *sdrC*, *sdrD*, *sdrE*) have been identified in *Staphylococcus aureus* that contain the dipeptide aspartic acid and serine (DS), encoded by an 18 bp repeat motif GAY TCN GAY TCN GAY AGY (SEQ ID NO: 15), where Y = pyrimidines and N = any base. This family of proteins has been named the Sdr's for serine-aspartic acid repeat. All of the 5 *S. aureus* *sdr* genes encode proteins that contain features that characterize them as surface associated proteins in Gram positive bacteria; namely at the N-terminus there is a secretory signal and at the C-terminus there are (i) several positive charged residues that serve as a stop signal for protein secretion, (ii) a hydrophobic transmembrane region and (iii) a wall-spanning region with an LPXTG motif that is required for accurate sorting and correct protein orientation in the cell wall. To identify novel genes that encode cell surface proteins in coagulase negative staphylococci we used the DS coding region of *clfA* as a gene probe to determine if homologs exist within various coagulase negative staphylococcal species. The coagulase negative staphylococcal species that we characterized were (1) *S. lugdunensis*, (2) *S. haemolyticus*, (3) *S. schleiferi* and (4) *S. epidermidis*. Each strain is listed below.